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Cost-effectiveness of the HepCATT intervention in specialist drug clinics to improve case-finding and engagement with HCV treatment for people who inject drugs in England

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ABSTRACT

Background and Aims People who inject drugs (PWID) are at high risk of hepatitis C virus (HCV) infection; however, ~50% are undiagnosed in England and linkage-to-care is poor. This study investigated the cost-effectiveness of an intervention (HepCATT) to improve case-finding and referral to HCV treatment compared with standard-of-care pathways in drug treatment centres in England. **Design** HCV transmission and disease progression model with cost-effectiveness analysis using a health-care perspective. Primary outcome and cost data from the HepCATT study parameterized the intervention, suggesting that HepCATT increased HCV testing in drug treatment centres 2.5-fold and engagement onto the HCV treatment pathway 10-fold. A model was used to estimate the decrease in HCV infections and HCV-related deaths from 2016, with costs and health benefits (quality-adjusted life-years or QALYs) tracked over 50 years. Univariable and probabilistic sensitivity analyses (PSA) were undertaken. **Setting** England-specific epidemic with 40% prevalence of chronic HCV among PWID. **Participants** PWID attending drug treatment centres. **Intervention** Nurse facilitator in drug treatment centres to improve the HCV care pathway from HCV case-finding to referral and linkage to specialist care. Comparator was the standard-of-care HCV care pathway. **Measurements** Incremental cost-effectiveness ratio (ICER) in terms of cost per QALY gained through improved case-finding. **Findings** Over 50 years per 1000 PWID, the HepCATT intervention could prevent 75 (95% central interval 37–129) deaths and 1330 (827–2040) or 51% (30–67%) of all new infections. The mean ICER was £7986 per QALY gained, with all PSA simulations being cost-effective at a £20 000 per QALY willingness-to-pay threshold. Univariable sensitivity analyses suggest the intervention would become cost-saving if the cost of HCV treatment reduces to £3900. If scaled up to all PWID in England, the intervention would cost £8.8 million and decrease incidence by 56% (33–70%) by 2030. **Conclusions** Increasing hepatitis C virus infection case-finding and treatment referral in drug treatment centres could be a highly cost-effective strategy for decreasing hepatitis C virus incidence among people who inject drugs.

Keywords Case-finding, cost-effectiveness, drug treatment centres, hepatitis C virus, mathematical modelling, people who inject drugs.

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INTRODUCTION

Globally, infection with hepatitis C virus (HCV) infection causes considerable morbidity [1]. Injecting drug use is the critical exposure in most developed countries [2]. In the United Kingdom, people who inject drugs (PWID) account for 90% of new reported cases [3]. HCV can now be easily cured with highly effective direct acting anti-viral treatments (DAAs) [4], motivating the World Health Organization (WHO) to set targets for eliminating HCV as a public health threat by 2030 [5,6]. The United Kingdom has adopted these targets [6] and has recently

agreed an elimination tender with pharmaceutical companies to enable this [7]. However, low diagnosis and linkage-to-care rates for PWID remain a key barrier to achieving these elimination targets in the United Kingdom and globally [3,8].

UK guidance recommends undertaking case-finding in specialist drug clinics [9,10], where a high yield of infection can be achieved [11]. However, during 2005–14, only 10% of cases identified in drug treatment centres were treated within a year, highlighting the need to improve the linkage-to-treatment in these settings. There are few studies investigating the cost-effectiveness of such interventions [9,12,13], most from the pre-DAA era. The Hepatitis C Awareness Through to Treatment study (HepCATT) showed that a nurse facilitator within drug treatment centres in three English settings could improve the HCV care pathway from HCV case-finding, referral and linkage to specialist care [14]. In this paper, we assess the cost-effectiveness of the HepCATT intervention compared to standard-of-care levels of testing and treatment among PWID in England. Insights from this analysis will be important for advocating for the further expansion of community-based case-finding and linkage-to-treatment interventions in the United Kingdom, some of which now include community-based treatment [15–18].

METHODS

The cost-effectiveness analysis compared the costs and impact of increased testing and engagement achieved among PWID through the HepCATT study in drug treatment centres to a counterfactual where the current standard-of-care levels of testing and engagement continues (*status quo*). The analysis was undertaken from a UK National Health Service (NHS) and Personal Social Services perspective, following National Institute for Health and Care Excellence (NICE) guidelines over a 50-year time horizon [19]. Personal Social Services include services not normally covered by the NHS [20], including drug treatment services and the HepCATT intervention being evaluated in this analysis. The analysis incorporated the health benefits of preventing long-term disease sequelae among individuals treated for HCV infection and onward transmission prevention benefits for other PWID. Costs (2018 GBP) and health utilities (quality-adjusted life years or QALYs) were attached to each disease stage, each discounted at 3.5% per year. The analysis follows broad best practice in clearly describing all details of the modelling, giving details of the derivation of all model parameters, calibrating and validating the model against available data, and incorporating parameter uncertainty [21,22]. The analysis did not follow a pre-registered analysis plan, but used similar methods to our previous studies [9,23].

Mathematical model

The cost-effectiveness analysis was conducted using an open dynamic model of HCV transmission and disease progression among current and former PWID, including diagnosis and treatment (see Fig. 1; model equations in Supporting information). The modelled population was stratified by whether or not individuals were receiving opioid substitution therapy (OST), which was used as a proxy for drug treatment centre attendance where HepCATT took place.

People who start injecting drugs enter the model as susceptible individuals not on drug treatment. Individuals become HCV-infected at a rate dependent on the prevalence of infection, with those on OST/drug treatment having a reduced risk of infection [24]. Newly infected individuals either spontaneously clear their infection (antibody-positive and RNA-negative) or become chronically infected (antibody and RNA-positive) (Fig. 1b), which is life-long unless treated. Upon primary infection, liver disease progression occurs as in Fig. 1c, with HCV-related death occurring from any stage after compensated cirrhosis. At any time, current injectors can initiate OST for an average duration and can die from drug-related mortality or permanently cease injecting. Cessation from injecting is assumed to be independent of OST based on long-term cohort data of PWID from the United Kingdom that showed no clear association [25]. Following cessation, individuals can no longer become HCV-infected, but can die due to natural causes and HCV (if infected) and can receive HCV treatment.

Chronically infected individuals can be diagnosed at a per-capita rate depending on rates of testing and are either lost to follow-up (LTFU) or engaged in the treatment pathway. Rates of testing depend on whether or not an individual is attending drug treatment. Engagement is defined as attending the hepatology clinic, whereupon they are treated at a per-capita rate and either achieve effective cure (sustained virological response, SVR) or fail treatment and continue to be chronically infected. Retreatment of those who fail treatment occurs at the same rate as for initial treatment. Disease progression continues at a decreased rate in cured individuals who have compensated or decompensated cirrhosis and ceases in those with milder disease [26,27]. Cured individuals can be re-infected at the same rate as for primary infection, whereupon disease progression continues from their current disease stage. Individuals who are LTFU are only re-engaged with the treatment pathway once they progress to compensated cirrhosis or more severe disease, or become in contact with HepCATT.

Figure 1 Schematic of the model structure for (a) population stratification by people who inject drugs (PWID) and harm reduction status, (b) infection, diagnosis and treatment and (c) disease progression

Parameterization and calibration of the standard-of-care model

The model was parameterized and calibrated to represent a generalized UK scenario using data from the annual unlinked anonymous monitoring (UAM) survey for PWID [28], baseline data collected for HepCATT [14] and HCV sentinel surveillance data collected from multiple testing settings [11]; see Table 1. The UAM survey gave us the mean HCV antibody prevalence (52%) among PWID in England and Wales for 2015 [28], or approximately 40% chronic prevalence [29]. Estimates suggest that 63% of PWID are currently on OST [28], with an average duration on OST of 8 months [30]. We assume stable OST coverage and HCV prevalence among PWID in recent years [28,31]. Based on a recent Cochrane systematic review, we assume being on OST reduces the risk of HCV transmission by 59% [24]. The percentage of chronically infected PWID who

Table 1 Demographic and epidemic model parameters.

Parameter description	*Point estimate*	*Sampled distribution*	*Rationale*	*Source*
Rate of cessation of injecting per year, set as 1/injecting duration	1/11.5	Injecting duration uniform [8,15]	Mean injecting duration 11.5 years, assumption for sampled range	[45]
Drug-related death rate per year	0.0073	Poisson distribution mean = 0.73/100	Data suggest 45–84 deaths per 10 000 person-years among opiate users identified from drug treatment and criminal justice records in England (2005–09)	[46]
Death rate among individuals who have ceased injecting (per year)	0.026	Life expectancy uniform (70, 80). Age at initiation of injecting uniform [20,30]	1/(life expectancy-age at initiation of injecting-injecting duration)	World Bank life expectancy data, UAM data
Initiation rate of new injectors (injectors per year)	Estimated through model calibration		Fitted assuming a constant population size of 1000 or UK population size and sampled death and cessation rates for current injectors	
Proportion of treated individuals who achieve SVR pre-2016	0.49	Uniform (0.483, 0.507)	UK SVR data from sentinel surveillance	[11]
Proportion of treated individuals that achieve SVR post-2016	0.93	Uniform (0.88, 0.98)	Results from SIMPLIFY Phase 4 trial using sofosbuvir and velpatisvir in people with recent injection drug use	[32]
Rate at which people start attending drug treatment centres (per year)	Estimated through model calibration		Fitted to give a coverage of OST (proportion of PWID currently on OST) that is uniformly sampled between 60–65% from unlinked anonymous monitoring survey	[40]
Rate at which people stop attending drug treatment centres (per year)	1/(years on OST)	Years on OST Uniform (0.33, 1)	Duration on OST was 8 months (4–12 months) in cohort of PWID in UK	[30]
Reduced risk of HCV transmission due to being on OST	0.41	Log-normal (0.22, 0.74)	Cochrane Review	[24]
HCV antibody prevalence	52%	Normal (CI = 51–55%)	From literature	[28]
Baseline transmission rate	Estimated through model calibration		Fitted using sampled antibody prevalence × (1-proportion of infections that spontaneously clear)	
Proportion of infections that spontaneously clear	0.26	Uniform (0.22, 0.29)	From literature	[29]
Rate at which individuals complete treatment = 1/treatment duration (per year)	52/12	Constant	12 weeks for DAA treatment	NICE guidelines

HCV = hepatitis C virus; UAM = unlinked anonymous monitoring survey; NICE = National Institute for Clinical Excellence; OST = opioid substitution therapy; DAA = direct acting antiviral treatments; CI = confidence interval; PWID = people who inject drugs; SVR = sustained virological response.

were diagnosed before the intervention was assumed to be 52% [28], with the standard-of-care testing rate at drug treatment centres (14% in last year) being estimated using baseline HepCATT data [14]. The testing rate outside drug treatment centres was estimated through model calibration. The standard-of-care rate of engagement with the treatment pathway following diagnosis at drug treatment centres was estimated using baseline HepCATT data and a study on the cascade of care for different testing settings in England [11]. The treatment rate for engaged individuals was estimated using baseline HepCATT data and was assumed to be the same, irrespective of where testing occurred. Although higher treatment rates may have been achieved recently, the data are uncertain and so are only considered in the sensitivity analysis. We assumed that the pre-2016 (pre-DAA) SVR was 49.5% [11] and the DAA SVR was 93% [32].

For the model calibration, 1000 parameter sets were sampled from the parameter distributions in Table 1. For each sampled parameter set, the transmission rate, OST recruitment rate and HCV testing rate for non-drug treatment settings were varied to fit the model (using MATLAB solver function lsqnonlin) to sampled values for the HCV chronic prevalence among current PWID in 2015, OST coverage and overall proportion diagnosed. This assumed that the system was in steady state before 2016. Only parameter sets where the proportion diagnosed was within its uncertainty range were accepted as model fits; the model was always able to fit to the HCV prevalence and OST coverage. The resulting 720 model fits were used to simulate the standard-of-care and intervention scenarios. The calibration process is described further in the Supporting information.

Standard-of-care comparator arm

The standard-of-care scenario assumes that testing, engagement and treatment are maintained at pre-HepCATT levels (Table 1) for individuals tested in all settings, with DAA therapy being undertaken in hospital clinics.

Intervention arm

Based on the results of the HepCATT study, we modelled an intervention scenario where the odds of testing in drug treatment centres increased 2.5-fold and the odds of engagement onto the treatment pathway increased 10-fold from 2016 [14]. We also assumed that individuals attending drug treatment centres that were previously LTFU could be re-engaged onto the treatment pathway at the same rate as those newly diagnosed due to the nurse liaison intervention. Parameter ranges for the standard-of-care and intervention scenarios are given in Table 2.

Impact analysis

The number of infections and disease-related deaths averted between 2016 and 2030 or 2066 were estimated by comparing the projections of the standard-of-care and HepCATT model scenarios. The relative difference in the incidence and prevalence of HCV by 2030 and the proportion of chronically infected PWID diagnosed was also estimated.

Costs and utility values

Costs and utilities from the literature are given in Supporting information, Table S7. Health utilities (QALYs) and HCV disease progression rates came from previous studies [26,27,33–35], with health utilities for HCV disease progression states [33] being multiplied by the baseline health utilities for PWID [36] or ex-PWID. Healthcare costs relating to HCV disease were taken from previous economic analyses [33,35]. Costs relating to the treatment pathway in hospitals using DAAs were based on the NHS treatment protocol (personal communication, Graham Foster; see Supporting information) and NHS reference costs [37]. Costs were inflated to 2018 GBP using the Health and Community Hospital Service pay and prices index [38].

Costs for the HepCATT intervention (improving testing and engagement) were calculated from time allocation and resource use (number of antibody and RNA tests) data collected (top-down approach) through interviews with nurses and key-workers involved in the intervention from two cities. Staff time was allocated to either administration and management costs, diagnosis costs or engagement costs. Nurse salaries came from study records. Key-worker salaries and overhead costs (rent, utilities) were obtained from the drug treatment provider (Addaction) undertaking the intervention. Management, overheads and training costs were assigned to give a fixed yearly cost, with a greater cost in the first year due to additional staff training. Peer-workers were volunteers, so opportunity costs were applied equivalent to the minimum key-worker salary. Dried blood spot testing costs were obtained from the laboratory, which was a cost incurred by the intervention. Costs for testing per patient were calculated by summing staff and resource costs for the diagnosis stage and dividing by the number tested. The costs of engagement per patient were calculated by summing engagement costs (for all referred individuals regardless of attendance) and dividing by the number of patients engaged in the treatment pathway. For HepCATT, this included costs for getting individuals to hospital appointments, including key-worker and

Table 2 Parameters related to HCV treatment pathway for the standard-of-care and intervention scenario.

Parameter	*Standard-of-care*	*Source*	*Intervention*	*Source*
Testing rate per year				
Drug treatment centres	0.140 (0.075–0.259)	HepCATT baseline data [14]	0.332 (0.167–0.586)	HepCATT intervention data; see Supporting information for more details [14]
Other settings and ex-injectors	Varied to give required proportion of injectors diagnosed (mean 52%) Posterior median 0.035 (0.001–0.450)		Same as for standard-of-care	Assume intervention has no impact on other settings
Engagement rate per year				
From drug treatment centres within 1 year of diagnosis	0.092 (0.035–0.242)	HepCATT baseline data [14]	0.741 (0.206–1.634)	HepCATT intervention data [14]
From other diagnosis settings within 1 year of diagnosis	0.092 (0.035–0.242)	HepCATT baseline data [14]	Same as for standard-of-care	
From drug treatment centres after 1 year since diagnosis	0 unless disease stage is F4 or above	Assumption that after 1 year patients are lost to follow-up until symptomatic	0.741 (0.206–1.634)	HepCATT intervention data [14]
From other settings after 1 year since diagnosis	0 unless disease stage is F4 or above	Assumption that after 1 year patients are lost to follow-up until symptomatic	Same as standard-of-care	Assume intervention has no impact on other settings
Treatment rate per year				
All settings	0.330 (0.170–0.590)	HepCATT baseline data [14]	Same as for standard-of-care	Assume intervention has no impact on treatment at hospital clinic
Proportion of treated individuals who achieve SVR post-2016	0.93	Uniform (0.88, 0.98)	Results from SIMPLIFY phase 4 trial using sofosbuvir and velpatisvir in people with recent injection drug use	[32]

HepCATT = Hepatitis C Awareness Through to Treatment study; SVR = sustained virological response; HCV = hepatitis C virus.

peer time, and for both arms included the costs of preliminary blood tests and fibroscan at the hospital. Costs for testing in other settings were taken from a published UK cost analysis of reflex testing [11], where samples are automatically tested for HCV RNA if they test antibody-positive. All testing was assumed to be reflex testing. Published costs for OST specialist prescribing were used, which incorporated staff time, prescribing costs and drug costs [38].

Cost-effectiveness analysis

Costs (2018 GBP, £1 = US$1.41) and health utilities were attached to each model state. The analysis used a 50-year time horizon to capture long-term effects of HCV infection and population prevention benefits of HCV treatment. The incremental cost-effectiveness ratio (ICER) was calculated as the difference in mean costs divided by the difference in mean QALYs between the intervention and the standard-of-care scenario. Cost-effectiveness was determined using the UK willingness-to-pay threshold of £20 000 per QALY gained [19].

Sensitivity analysis

A probabilistic sensitivity analysis (PSA) was performed for both modelled scenarios, and cost-effectiveness acceptability curves were plotted. The impact of parameter uncertainty on the incremental costs and QALYs was assessed

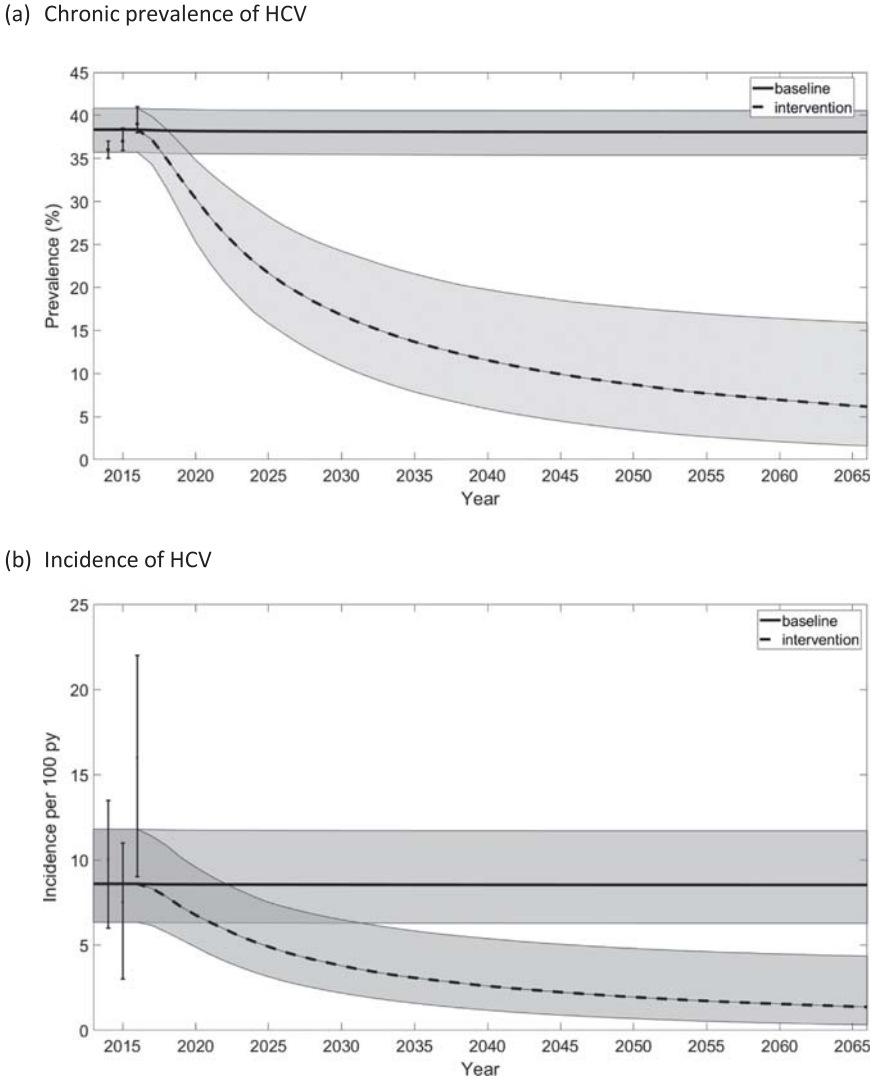

Figure 2 Model projections of the (a) chronic prevalence and (b) incidence of hepatitis C virus (HCV) with and without the costs sampled from uniform distributions. Assumes population size of 1000 people who inject drugs. Hepatitis C Awareness Through to Treatment study (HepCATT) intervention, with data on the prevalence of HCV in 2016 (which the model was fitted to) and incidence of HCV for 2015 and 2016 (which the model was not fitted to) being shown for comparison. Points are the mean of the data estimates with the whiskers showing the 95% confidence intervals. The black solid or dashed lines show the median of the model projections with the shaded areas denoting the 95% central range of the model projections

Table 3 Costs related to testing and linkage to treatment.

Step		*Standard-of-care cost*	*Intervention cost*	*Source*
HepCATT start-up cost for first year including management staff time during project initiation, nurse staff training and peer worker training		0	(£25 403–£34 712)	HepCATT costing analysis (see Supporting information)
Second and subsequent years fixed costs for HepCATT includes management, staff project oversight and one round of peer worker training		0	(£10 951–£13 818)	
Costs per test (includes staff time and test costs)	Antibody-negative	£53 ± 10%	(£106–161)	[11] and HepCATT costing analysis (see Supporting information)
	Antibody-positive	£119 ± 10%	(£150–212)	
	Previous known SVR (antibody^{+})	£119 ± 10%	(£146–207)	
Costs per engagement (includes staff referral costs and preliminary blood tests and fibroscan at the hospital)	From diagnosed	£409 ± 10%	(£124–212) (referral cost) + (£332 ± 10%) (at hospital)	Standard-of-care referral costs from [11], hospital costs from expert opinion (personal communication, Graham Foster) Intervention referral costs from HepCATT costing analysis (see Supporting information)
	From lost to follow-up	£409 ± 10% (later stages of disease progression only)	(£96–124) (identifying patient) + (£124–212) (referral cost) + (£332 ± 10%) (at hospital)	
Cost per treatment	Treatment monitoring	£394 ± 10%		Expert opinion (personal communication, Graham Foster, and see Supporting information for details)
	Weekly drug cost	£3249 ± 10%		Assume full current list price [47]

Costs sampled from uniform distributions. Assumes population size of 1000 people who inject drugs. HepCATT = Hepatitis C Awareness Through to Treatment study; SVR = sustained virological response.

using an analysis of covariance (ANCOVA) analysis across the model fits [39].

Matched univariable sensitivity analyses examined the effect of:

(a) varying the time horizon (100 or 15 years compared to 50 years) or discount rate (0 and 6 compared to 3.5%) across a wide range, as recommended by NICE;
(b) reducing the HCV drug cost by 80% (£7796 per 12-week treatment course) to typify what the current cost of treatment in England could be, although the actual price is unknown;
(c) increasing the treatment rate from engagement in all settings to 80% (from 16 to 45%) within a year to determine how increased treatment uptake may affect the cost-effectiveness of the intervention; and
(d) varying chronic HCV prevalence to 20 or 60% (compared to 40%) to capture the range of HCV prevalences observed in different UK or international settings [40,41].

The impact of decreasing drug costs was also investigated in a threshold analysis, whereby the mean ICER was calculated for different drug costs to determine at what price the intervention becomes cost-saving. Finally, an expected value of perfect information (EVPI) analysis was carried out [39] at the current full list DAA price.

RESULTS

Impact analysis

The intervention is estimated to increase the number of PWID tested annually twofold [95% credible interval (CrI) = 1.5–2.5] and the number treated 2.9-fold (95% CrI = 2.3–6.1) (Supporting information, Fig. S1). This increase in treatment is estimated to avert 75 deaths (95% CrI = 37–129), 1330 infections (95% CrI = 827–2040) and gain 1607 QALYs over 50 years per 1000 PWID, or in England assuming 139 830 PWID [42] then it would avert 10 487 deaths (95% CrI = 5174–18 038), 185 974 infections (95% CrI = 115 639–285 253) and gain 224 707 QALYs. This equates to 64% (95% CrI = 50–72%) of all HCV-related deaths and 51% (95% CrI = 30–67%) of all infections being averted over this period and a 56% (95% CrI = 38–70%) decrease in chronic HCV prevalence and incidence by 2030 (Fig. 2). The number of disease related deaths decreased by 29% (95% CrI = 20–39%) during the same period.

Costs of the intervention

There was one half-time nurse liaison associated with each setting during the intervention. Involvement of key worker staff varied among settings, with one key worker supervising the peer workers for between 1 or 2 days a week. The remaining key-workers at the two settings each had 1–1-.5 days of training for HepCATT. In one setting, there were nine key-workers who each spent 0.03 full-time equivalent (FTE) or 0.28 FTE altogether on HepCATT and six peers who spent 0.14 FTE altogether. In the second setting, there were 48 key-workers and 15 peers totalling 0.38 FTE and 0.5 FTE, respectively. Table 3 shows the allocation of HepCATT costs to different stages of the diagnosis and engagement pathway; Supporting information, Table S8 gives a breakdown of standard-of-care costs. Once set up, the ongoing yearly fixed costs of HepCATT are £12 385 (including one round of peer worker training), while the average cost to engage a previously undiagnosed or diagnosed patient into treatment is £682 and £600, respectively. All stages of the pathway to engagement are more costly than the standard-of-care, reflecting the increased staff time associated with HepCATT.

The breakdown of costs applied over the 50-year time horizon per 1000 PWID are shown in Table 4. The total incremental cost of the intervention was £12.8 million for the full list drug price. This was made up of extra expenditure (£15.8 million), mainly in testing and engagement (HepCATT, £1.0 million) and HCV treatment (PWID and ex-injectors, £14.8 million) and cost savings (£3.0 million) in HCV-related health-care costs. For the England population of PWID, the incremental costs increase to £1789.8 million for the full price of DAAs, with the intervention costing £144.8 million over 50 years or £8.8 million to 2030 (discounted). The annual intervention cost is more

Table 4 Breakdown of discounted costs over 50-year time horizon.

	Standard-of-care mean	*Intervention mean*	*Difference*
HCV-related health care	£9 306 667	£6 261 626	–£3 045 041
HCV treatment ex-PWID	£3 318 512	£5 001 366	£1 682 854
HCV treatment PWID	£1 894 516	£14 998 725	£13 104 208
Testing and engagement[a]	£424 988	£1 460 213	£1 035 225
OST	£48 078 808	£48 137 935	£59 127
Total	£63 023 491	£75 859 865	£12 836 374

[a]Includes cost of testing and engagement in drug treatment centres and other settings and testing and engagement of ex-injectors. Initial population size of PWID is 1000, injector population is maintained at 1000, with people ceasing injecting also followed for the 50-year time horizon. HCV = hepatitis C virus; PWID = people who inject drugs; OST = opioid substitution therapy.

than the standard-of-care scenario until 2048 (Supporting information, Fig. S2).

Base case cost-effectiveness analysis

Table 5 shows the results of the cost-effectiveness analysis over 50 years. For the full list DAA price, the intervention costs £12.8 million more than the standard-of-care scenario but accrues 1607 extra QALYs, giving a mean ICER of £7986 per QALY gained. The cost-effectiveness plane (Supporting information, Fig. S3) shows that all simulations are below the £20 000 per QALY willingness-to-pay threshold.

Sensitivity analysis

The results were robust to numerous univariable sensitivity analyses, with the ICER remaining below the £20 000 per QALY willingness-to-pay threshold (Fig. 3). Decreasing the discount rate, lengthening the time horizon or reducing the HCV treatment drug cost by 80% all decreases the mean ICER, making the intervention more cost-effective. Indeed, an 80% decrease in drug cost causes the total incremental cost of the intervention to reduce to £1 145 245 per 1000 PWID, or £160 139 908 for an England population of 139 830 PWID. Similarly, increasing the proportion of engaged individuals that start treatment to 80% (from 16 to 45%) decreases the ICER to £4321 per QALY gained, and achieves a 77% (95% CrI = 57–87%) reduction in incidence by 2030. Assuming a lower chronic HCV prevalence (20%) does not greatly affect the ICER (£5692 per QALY), while assuming higher chronic prevalence (60%) increases the ICER to £17 797 per QALY.

The threshold analysis (Supporting information, Fig. S4) shows that the intervention becomes cost-saving (costs less than the standard-of-care comparator and saves more QALYs) for a 90% reduction in drug price (£3898 per 12-week regimen). The ANCOVA (Supporting information, Fig. S5) shows that uncertainty in the annual HCV-related health-care costs accounted for 80% of the variation in incremental costs, while uncertainty in the treatment rate and utility values for mild disease (F0–F1) resulted in 59% of the variability in incremental QALYs. The EVPI was zero, as all simulations are cost-effective at the £20 000 per QALY willingness-to-pay threshold.

DISCUSSION

Introducing a nurse-led intervention (with peer support) to improve the HCV testing and engagement to care of PWID

Table 5 Cost-effectiveness results (initial population size 1000 current injectors).

	Mean total costs	*Incremental costs*	*Mean total QALYs*	*Incremental QALYs*	*Mean ICER (£ per QALY)*
Standard-of-care	£63 023 491		36 865		
Intervention	£75 859 865	£12 836 374	38 472	1607	£7986

QALY = quality-adjusted life year; ICER = incremental cost-effectiveness ratio.

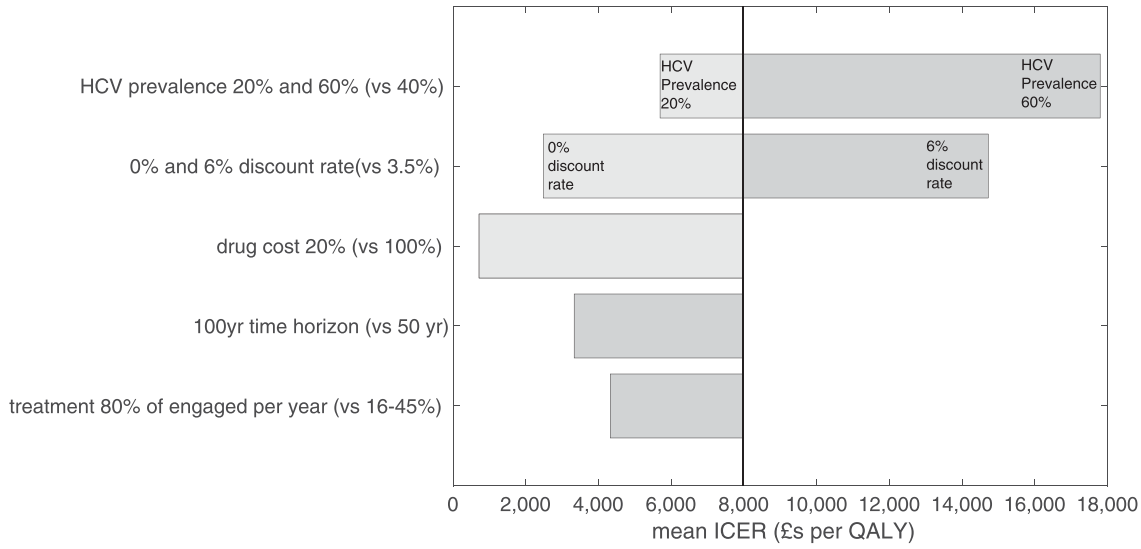

Figure 3 Tornado plot showing the effect of changing different model assumptions on the mean incremental cost-effectiveness ratio (ICER) with increased parameters in the darker shade of grey

attending drug treatment centres is cost-effective (£7986 per QALY saved) at current list prices for DAA HCV treatment (£39 000 per treatment), and becomes cost-saving if drug costs decrease to £3900 per treatment. Moreover, if the intervention were scaled-up to all drug treatment centres in England it could avert 51% of infections and 64% of HCV-related deaths over a 50-year period and reduce incidence by 56% by 2030. Optimizing the intervention further, with 80% of people being treated within a year of engagement results in the intervention becoming more cost-effective (£4321 per QALY for full list price of DAAs) and could reduce incidence by 77% by 2030. Because most ongoing HCV transmission in the United Kingdom is among PWID [2], these impact projections suggest that this intervention could be an important component of the NHS England initiative to reach the WHO elimination targets of decreasing HCV incidence by 90% by 2030 or earlier. National estimates for scaling-up the intervention suggest that it would cost £144.8 million during the next 50 years, or £8.8 million by 2030 (discounted).

Strengths and limitations

The main strength of our study is that we evaluated a real-life intervention using empirical data on the outcomes of the intervention and costs. We also used a dynamic HCV transmission model to capture the prevention benefits of the intervention, while incorporating uncertainty in all model parameters. Nonetheless, potential limitations still exist.

First, the estimates for fixed intervention costs, which include management (staff time and building costs) and training costs, are based on two of the three study settings. This was deemed appropriate because these two settings were of differing sizes in terms of PWID population but still had similar set-up costs.

Secondly, a generic English setting was modelled to make our results relevant to the whole of England. However, OST coverage and HCV prevalence vary throughout England and the intervention's cost-effectiveness may depend on these inputs. Indeed, the cost-effectiveness of the intervention diminishes at higher chronic HCV prevalences (60%) due to greater re-infection [43], although it is still cost-effective. In contrast, variation in the coverage of OST (proportion of PWID currently on OST) is unlikely to affect the cost-effectiveness of the intervention, with the uncertainty included in our analysis (60–65%) not effecting our results. However, the impact of the intervention will be lessened at lower OST coverage levels because the reach of the case-finding strategy will be reduced. This could also occur if many PWID inject stimulants for which OST is not an effective intervention.

Lastly, the analysis used data on the overall proportion of PWID diagnosed with HCV to obtain a testing rate in settings other than drug treatment centres. Although a wide range of testing rates was used (0.01–0.45 per year) in the standard-of-care comparator, it is likely that testing rates have increased across all services because of the ongoing expansion of HCV treatment. It is unclear how this will affect the cost-effectiveness of this intervention, although solely improving the proportion of engaged individuals that start treatment improves the cost-effectiveness of the intervention in our sensitivity analyses.

Comparison with other studies

This is the first UK and European study to evaluate the cost-effectiveness of a real-life case-finding intervention among PWID since the emergence of DAA therapies. Our findings are consistent with other studies, which find case-finding among PWID to be cost-effective when sufficient diagnosed individuals are treated [9,12,13,44], with some of these interventions also providing on-site HCV treatment in drug treatment centres to improve linkage to treatment [45]. Only two of these studies considered the use of new DAA therapies [12,44], finding that HCV screening through drug treatment centres with active linkage to treatment was cost-effective in New York city (< $35 000 per QALY gained). Two other European studies before the emergence of DAA therapies considered the cost-effectiveness of case-finding interventions for PWID, with both including scenarios that assumed the use of a 'DAA-like' treatment with higher drug cost and SVR. One UK study found that introducing dried blood spot testing in drug treatment centres was cost-effective at less than £15 000 per QALY when assuming the use of interferon-based treatments or first generation DAAs [9]. Another study from the Netherlands evaluated testing in drug treatment centres (comparator was no testing), finding it to be similarly cost-effective (€9056 per QALY) to our intervention (at full list price). However, they assumed that 77% of diagnosed cases were referred and 37% of these cases were treated [13], considerably higher than we assumed for our analysis.

Conclusions and implications

Drug treatment centres are a high-yield setting for identifying individuals who require HCV treatment [11]. Our study provides evidence that introducing HCV nurse facilitators in drug treatment centres is highly cost-effective, potentially cost-saving if HCV drug prices fall sufficiently, and if scaled-up could reduce HCV incidence by 56% by 2030 for an estimated direct intervention cost of £8.8 million if scaled-up nationally. This could contribute considerably to national targets for achieving HCV elimination as a public health problem. Better engagement and therefore greater impact could be achieved if this intervention also

provides HCV treatment on-site, as has been piloted in other settings [15].

Declaration of interests

M.H. reports personal fees from Gilead, Abbvie and MSD. P. V. has received unrestricted research grants from Gilead and honoraria from Gilead and Abbvie. N.K.M. has received unrestricted research grants and honoraria from Gilead and Merck. The other authors declare no conflicts of interest.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1 Supporting Information.